Practice variations in managing infantile hemangiomas

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Abstract

Background Infantile hemangioma (IH) is the most common benign tumor of infancy. For children with IH who require treatment, propranolol and other beta blockers have been shown to be safe and effective. Although consensus guidelines for propranolol have been published, anecdotal experience suggests that there remain variations in management. This study was performed to document these variations amongst providers and to identify areas for future research. **Methods** We conducted an internet-based survey of clinicians who treat patients with IH. Characteristics of respondents were collected. Hypothetical cases and management scenarios were presented and respondents were ask to comment on dosing, monitoring, frequency of follow-up, duration of therapy, whether to taper or abruptly discontinue mediation, and which patients should get additional evaluation. **Results** Twenty-nine respondents participated in the survey: pediatric hematologists/oncologists (n= 15), pediatric cardiologists (n= 10), dermatologists (n = 2), an ophthalmologist (n = 1), and a neonatologist (n = 1). Most respondents use generic propranolol in infants with growing IH of the head and neck, with a goal dose of 2 mg/kg/day, until approximately one year of age. A variety of management strategies were documented including which patients should be treated, optimal dose and duration of therapy, how patients should be monitored, which patients should get additional work up, how propranolol should best be discontinued, and how often to see patients in follow-up. **Conclusions** This study demonstrates wide practice variations in managing patients with infantile hemangioma. Further research is indicated to address these variations and develop additional/updated evidence-based guidelines.

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Abbreviations:

IH	infantile hemangioma
CGA	corrected gestational age
CPG	clinical practice guideline
PHO	pediatric hematologist/oncologist
FDA	Food and Drug Administration

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Methods

We conducted an internet-based survey of clinicians who treat patients with IH. Characteristics of respondents were collected. Hypothetical cases and management scenarios were presented and respondents were ask to comment on dosing, monitoring, frequency of follow-up, duration of therapy, whether to taper or abruptly discontinue mediation, and which patients should get additional evaluation.

Results

Twenty-nine respondents participated in the survey: pediatric hematologists/oncologists (n= 15), pediatric cardiologists (n= 10), dermatologists (n = 2), an ophthalmologist (n = 1), and a neonatologist (n = 1). Most respondents use generic propranolol in infants with growing IH of the head and neck, with a goal dose of 2 mg/kg/day, until approximately one year of age. A variety of management strategies were documented including which patients should be treated, optimal dose and duration of therapy, how patients should be monitored, which patients should get additional work up, how propranolol should best be discontinued, and how often to see patients in follow-up.

Conclusions

This study demonstrates wide practice variations in managing patients with infantile hemangioma. Further research is indicated to address these variations and develop additional/updated evidence-based guidelines.

Introduction

Infantile hemangioma (IH) is the most common benign tumor of infancy. IH typically appears shortly after birth and proliferates over several months. IH growth usually plateaus by 9 – 12 months of age, followed by spontaneous involution over months to years.[1] The majority of IH are small and many patients require no treatment. However, IH can cause morbidity including ulceration (with or without infection), mass effects related to location (such as respiratory difficulties from airway lesions), and disfigurement. Thus, many patients benefit from treatment.[2] Following the first report in 2008,[3] the use of propranolol has revolutionized the treatment of IH. Multiple clinical trials and case series have since documented propranolol's safety and efficacy.[4-12] Hemangeol®, a pediatric formulation of propranolol to treat patients with IH at least 5 weeks old by corrected gestational age (CGA), was approved by the United States Food and Drug Administration (FDA) in 2014.[13]

Despite a surge of publications about propranolol therapy for IH, many questions remain unanswered. A consensus conference report (co-authored primarily by dermatologists) published in 2013 acknowledged "significant uncertainty and divergence of opinion regarding safety monitoring and dose escalation for propranolol use in IH."[14] In addition to monitoring and dose escalation, other issues with limited evidence include the optimal dose of propranolol, duration of therapy, the upper and lower age limits for treating children with IH, how often to see patients in follow-up, which patient should get additional work up (such as an echocardiogram), and how propranolol should best be discontinued (tapered or stopped abruptly).

A clinical practice guideline (CPG) for the management of IH was published by the American Academy of Pediatrics in January 2019.[15] It summarized the literature through January 2017 and provided evidence-based key action statements along with supporting levels of evidence and strengths of recommendation. Because propranolol is a nonselective antagonist of beta-adrenergic receptors and is known to lower heart rate and blood pressure, many primary care providers remain hesitant to prescribe it for infants (unpublished observations). Therefore, referrals are often made to pediatric hematologists/oncologists (PHO), dermatologists, plastic surgeons, cardiologists, or other hemangioma experts when therapy with propranolol is being considered. Indeed, the CPG suggests that, "depending on the clinician's comfort level and local access to specialty care," infants considered to have high risk IH may "require a higher level of experience and expertise to determine if additional intervention is indicated."[15] An electronic tool has been developed and validated to help primary care providers decide which patients with IH need treatment and/or referral.[16]

We hypothesized that there is wide variation amongst clinicians within specialties and between specialties in how they treat and monitor patients with IH. Many of the potential variations could have an impact on cost, anxiety, and family issues such as time off work. The objective of this study was to document these variations, and to identify areas for additional research.

Methods

To better quantify and understand practice variations, we conducted an internet-based survey of clinicians

from a range of specialties who treat patients with IH. The survey contained 47 questions, many of which were multiple choice and allowed multiple answers ("select all that apply"). Most questions had free text boxes where comments could be made. An invitation and link to complete this voluntary survey was posted on two listservs of the American Society of Pediatric Hematology/Oncology: a Clinical Forum Digest as well as a listserv for the Vascular Anomalies Special Interest Group. In addition, email invitations were sent to personal contacts in dermatology, cardiology, plastic surgery, pediatric otolaryngology, pediatric ophthalmology, and general pediatrics. Forwarding and sharing of the survey link to appropriate providers was encouraged. In addition, if a provider was not the best person to complete the survey, they were encouraged to forward the invitation to the person or discipline who treats the most patients with IH at that institution. Multiple responses per institution were encouraged. Because the survey link was posted on listservs and liberally forwarded, we cannot determine the number of clinicians who received or saw the link. Thus, the response rate is unknown. The survey was created and administered using REDCap.[17] The survey was active from October 2021 until May 2022. Descriptive statistics were used to analyze results. No protected health information was obtained. This study was approved by the Institutional Review Board at Atrium Health Wake Forest Baptist Medical Center in Winston-Salem, North Carolina (USA).

Results

Twenty-nine respondents participated in the survey. The characteristics of the respondents are shown in Table 1. The majority of respondents (51.7%) were PHOs from North America, with pediatric cardiology (34.5%) being the second largest group. One respondent was from Asia. Of the 28 responses from North America, 16 states were represented. At respondents' institutions, the majority of patients with IH are treated by PHOs and dermatologists.

A summary of key responses is shown in Table 2. Hypothetical cases and management scenarios are shown in Table 3. From the responses, several specific observations and several generalizations can be made. The decision to observe or treat is subjective. Shared decision making with the parent(s) is commonly employed. When treatment is deemed indicated, propranolol is the most commonly used first-line treatment. Respondents are more likely to treat IH on the head or neck than the trunk or extremities. For uncomplicated patients at least 5 weeks old by CGA, most are treated as outpatients. The decision on which patients to admit for monitoring varies widely and includes indications such as those with PHACE syndrome; those less than 5 weeks CGA; patients with ulcerated, painful, or bleeding hemangiomas; and patients with perceived high risk social situations. Many respondents will treat infants less than 5 weeks CGA, especially if an IH is on the head/neck and/or causing problems (such as ulceration or bleeding). A majority (83%) would monitor those patients (< 5 weeks CGA) more closely than older patients (> 5 weeks CGA), usually (58.6%) in the hospital. For infants > 5 weeks CGA who are otherwise healthy and have a reassuring history and exam, the majority (63%) of respondents administer the first dose of propranolol under medical supervision (e.g. in the clinic or hospital). The period of observation ranges from 1 hour to overnight, and longer for high risk/complicated patients. Heart rate and blood pressure are the most common values monitored. Most respondents (74%) obtain a liver ultrasound if 5 or more cutaneous IH are present. Approximately 40% of providers do not have an upper age limit for treatment. For patients without PHACE syndrome or other risk factors for toxicity, a minority of respondents obtain lab work, an electrocardiogram, an echocardiogram, or a cardiology consult prior to starting treatment. The majority (88.9%) of respondents take baseline photographs for the patient's electronic medical records. Most clinicians (71%) prescribe generic propranolol rather than trade name propranolol (Hemangeol®). Propranolol is perceived to be very easy to obtain including coverage by the patient's insurance and/or only a small copay. The most common goal dose for propranolol is 2 mg/kg/day, divided twice a day, and the full dose is most commonly reached (via escalating dose) at 2 weeks of therapy. The perceived discontinuation rate of propranolol due to side effects is less than 10%. Respondents infrequently (7.7%) switch from one form of propranolol (generic to trade name, or vice versa) due to side effects. On-therapy and off-therapy practices vary considerably. A minority of providers (26.9%) have started propranolol using a telehealth encounter only. However, a majority (64%) are using telehealth for routine follow-up visits. A majority of respondents (63%) provide oral syringes and instruct the parents on the prescribed dose. A variety of educational tools are used, although few specific websites are recom-

mended. Most respondents (57.7%) discontinue propranolol at approximately 1 year of age for typical cases (although each patient is considered unique). When discontinuing propranolol, the majority of respondents (53.8%) taper it, typically over 2 to 4 weeks; 26.9% let the patient outgrow the dose and then stop it at some point in the future; 15.4% discontinue it abruptly. The majority of respondents (65%) reassess patients in clinic at least once after discontinuing propranolol, presumably to assess for rebound growth.

Discussion

This study documented a wide variation in the treatment of infantile hemangiomas. A consistent theme is that each patient and each IH are unique. The clinical practice guidelines are based on available data, and on expert opinions in the absence of data. With the publication of additional high quality studies and the widespread use of beta blockers for the management of IH, updated clinical practice guidelines may be indicated.

Ongoing studies continue to demonstrate the safety and efficacy of propranolol as well as other beta-blockers including atenolol,[18,19] nadolol,[20] and topical timolol.[21] Most studies have used a goal dose of 2 – 3 mg/kg/day of propranolol.[15] Three mg/kg/day is superior to 1 mg/kg/day,[9] but little data exist comparing 2 mg/kg/day to 3 mg/kg/day.[22] In fact, doses of 2.5 – 3 mg/kg/day may increase toxicity without added benefit.[12,23,24] Early initiation of propranolol (before 10 – 12 weeks of age) improves outcomes compared to an older age of initiation.[25,26] Current literature suggests that propranolol is effective and well tolerated in infants younger than five weeks corrected gestational age.[27] Depending on response, most experts recommend continuing propranolol until age 12 months, and sometimes longer.[15,28] The CPG recommends a baseline echocardiogram for patients with PHACE syndrome, but does not address the indications of an echocardiogram for other patients.[15] Obtaining a baseline electrocardiogram is rarely helpful in otherwise well infants.[29] Five or more cutaneous IH is associated with IH of the liver, and it has been recommended that such patients undergo ultrasound of the liver.[30] However, at least one study found that liver ultrasound rarely affects clinical management, and that it may be safely omitted in the absence of concerning signs or symptoms such as lethargy or poor feeding.[31]

The FDA's recommendation for monitoring patients is currently based on a clinical trial which had strict criteria and oversight, including intermittently monitoring heart rate and blood pressure for two hours after the first dose and when increasing the dose.[9]For propranolol, peak plasma concentrations occur 1 – 4 hours after a dose. Consumption of protein-rich foods increases the bioavailability by about 50% with no change in time to peak concentration.[32] At least one large study suggests that at home initiation and dose escalation may be safely done.[33] In addition, guidelines from Britain, Australia, and North America state that in children without risk factors, outpatient initiation without monitoring may be safely done with initial doses of 1 mg/kg/day.[34-36] At home initiation and dose escalation, including by telehealth encounters, became more common for non-high risk patients during the COVID-19 pandemic.[34] When therapy has been completed, some clinicians may discontinue propranolol abruptly,[36]although it has been suggested that it be tapered (for example, over two to four weeks), to potentially lower the risk of rebound growth.[28,37] Despite evidence that most patients can be safely started on propranolol at home, many practitioners continue to monitor patients in the clinic or in the hospital when initiating or increasing the dose of propranolol, and some still get routine cardiac assessments and lab work.

Areas identified for future research and discussion include the optimal dose of propranolol (including for ulcerated IH, which may respond better to a lower initial dose ([?]1 mg/kg/day) of propranolol[38]), the optimal duration of therapy, which patients truly benefit from ultrasound of the liver, how patients should be monitored, how often to see patients in follow-up, which patients should get additional work up (such as an echocardiogram), and how propranolol should best be discontinued (tapered or stopped abruptly).

Limitations of this study include a small sample size which is heavily biased towards PHOs and pediatric cardiologists. Few dermatologists and other providers responded, which could impact results since dermatologists, particularly the Hemangioma Investigators Group (https://www.hemangiomaeducation.org/) have been leaders in the treatment of infantile hemangiomas. Thus, analysis of variations in practice be-

tween specialties could not be reliably performed. Published guidelines suggest that dermatologists are more comfortable with outpatient initiation and dose escalation of beta blockers.[34-36]

In conclusion, this study demonstrates wide practice variations in managing infantile hemangiomas. Further research is indicated to address these variations and develop additional/updated evidence-based guidelines.

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References

1. Leaute-Labreze C, Harper JI, Hoeger PH. Infantile haemangioma.*Lancet* 2017;390:85-94.

2. Pahl KS, McLean TW. Infantile Hemangioma: A Current Review. *J Pediatr Hematol Oncol* 2022;44:31-9.

3. Leaute-Labreze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo JB, Taieb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med* 2008;358:2649-51.

4. Aly MM, Hamza AF, Abdel Kader HM, Saafan HA, Ghazy MS, Ragab IA. Therapeutic superiority of combined propranolol with short steroids course over propranolol monotherapy in infantile hemangioma. *Eur J Pediatr* 2015;174:1503-9.

5. Darrow DH, Greene AK, Mancini AJ, Nopper AJ. Diagnosis and Management of Infantile Hemangioma. *Pediatrics* 2015;136:e1060-104.

6. Hoeger PH, Harper JI, Baselga E, et al. Treatment of infantile haemangiomas: recommendations of a European expert group. Eur J Pediatr 2015;174:855-65.

7. Hogeling M, Adams S, Wargon O. A randomized controlled trial of propranolol for infantile hemangiomas. *Pediatrics*2011;128:e259-66.

8. Leaute-Labreze C, Boccara O, Degrugillier-Chopinet C, et al. Safety of Oral Propranolol for the Treatment of Infantile Hemangioma: A Systematic Review. *Pediatrics* 2016;138.

9. Leaute-Labreze C, Voisard JJ, Moore N. Oral Propranolol for Infantile Hemangioma. *N Engl J Med* 2015;373:284-5.

10. Tian Y, Xu DP, Tong S, Xi SL, Liu ZM, Wang XK. Oral Propranolol for the Treatment of Infantile Hemangiomas in the Post-Proliferative Phase: A-Single Center Retrospective Study of 31 Cases. *J Oral Maxillofac Surg* 2016;74:1623-9.

11. Baselga E, Dembowska-Baginska B, Przewratil P, et al. Efficacy of Propranolol Between 6 and 12 Months of Age in High-Risk Infantile Hemangioma. *Pediatrics* 2018;142.

12. Droitcourt C, Kerbrat S, Rault C, et al. Safety of Oral Propranolol for Infantile Hemangioma. *Pediatrics* 2018;141.

13. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205410Orig1s000TOC.cfm. Accessed May 28, 2023.

14. Drolet BA, Frommelt PC, Chamlin SL, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference.*Pediatrics* 2013;131:128-40.

15. Krowchuk DP, Frieden IJ, Mancini AJ, et al. Clinical Practice Guideline for the Management of Infantile Hemangiomas. *Pediatrics*2019;143.

16. Leaute-Labreze C, Baselga Torres E, Weibel L, et al. The Infantile Hemangioma Referral Score: A Validated Tool for Physicians.*Pediatrics* 2020;145.

17. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners.*J Biomed Inform* 2019;95:103208.

18. Chen T, Gudipudi R, Nguyen SA, Carroll W, Clemmens C. Should Propranolol Remain the Gold Standard for Treatment of Infantile Hemangioma? A Systematic Review and Meta-Analysis of Propranolol Versus Atenolol. *Ann Otol Rhinol Laryngol* 2023;132:332-40.

19. Pattanshetti SA, Mahalmani VM, Sarma P, et al. Oral Atenolol versus Propranolol in the Treatment of Infantile Hemangioma: A Systematic Review and Meta-Analysis. *J Indian Assoc Pediatr Surg*2022;27:279-86.

20. Pope E, Lara-Corrales I, Sibbald C, et al. Noninferiority and Safety of Nadolol vs Propranolol in Infants With Infantile Hemangioma: A Randomized Clinical Trial. *JAMA Pediatr* 2022;176:34-41.

21. Moehrle M, Leaute-Labreze C, Schmidt V, Rocken M, Poets CF, Goelz R. Topical timolol for small hemangiomas of infancy. *Pediatr Dermatol* 2013;30:245-9.

22. Krowchuk DP, Frieden IJ, Mancini AJ, et al. Clinical Practice Guideline for the Management of Infantile Hemangiomas. *Pediatrics*2019;143(1):e20183475.

23. Huang AH, Mannschreck D, Aggarwal P, Mahon M, Cohen BA. Retrospective case series of increased oral propranolol dosage for infantile hemangiomas. *Pediatr Dermatol* 2020;37:1057-62.

24. Yang H, Hu DL, Shu Q, Guo XD. Efficacy and adverse effects of oral propranolol in infantile hemangioma: a meta-analysis of comparative studies. *World J Pediatr* 2019;15:546-58.

25. Giachetti A, Diaz MS, Boggio P, Posadas Martinez ML. Early propranolol treatment of infantile hemangiomas improves outcome.*An Bras Dermatol* 2023;98(3):310-315.

26. Leaute-Labreze C, Frieden I, Delarue A. Early initiation of treatment with oral propranolol for infantile hemangioma improves success rate. *Pediatr Dermatol* 2023;40(2):261-264.

27. Gatts JE, Rush MC, Check JF, Samelak DM, McLean TW. Safety of propranolol for infantile hemangioma in infants less than five weeks corrected age. *Pediatr Dermatol* 2022;39:389-93.

28. Shah SD, Baselga E, McCuaig C, et al. Rebound Growth of Infantile Hemangiomas After Propranolol Therapy. *Pediatrics* 2016;137.

29. Streicher JL, Riley EB, Castelo-Soccio LA. Reevaluating the Need for Electrocardiograms Prior to Initiation of Treatment With Propranolol for Infantile Hemangiomas. *JAMA Pediatr* 2016;170:906-7.

30. Horii KA, Drolet BA, Frieden IJ, et al. Prospective study of the frequency of hepatic hemangiomas in infants with multiple cutaneous infantile hemangiomas. *Pediatr Dermatol* 2011;28:245-53.

31. Mahon C, McHugh K, Alband N, et al. Routine liver ultrasound screening does not alter clinical management in a cohort study of multiple cutaneous infantile haemangioma. *Br J Dermatol*2021;184:340-1.

32. chrome extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.accessdata.fda.gov/ drugsatfda_docs/label/2014/205410s000lbl.pdf. Accessed June 1, 2023.

33. Chang L, Ye X, Qiu Y, et al. Is Propranolol Safe and Effective for Outpatient Use for Infantile Hemangioma? A Prospective Study of 679 Cases From One Center in China. *Ann Plast Surg* 2016;76:559-63.

34. Frieden IJ, Puttgen KB, Drolet BA, et al. Management of infantile hemangiomas during the COVID pandemic. *Pediatr Dermatol*2020;37:412-8.

35. Smithson SL, Rademaker M, Adams S, et al. Consensus statement for the treatment of infantile haemangiomas with propranolol.*Australas J Dermatol* 2017;58:155-9.

36. Solman L, Glover M, Beattie PE, et al. Oral propranolol in the treatment of proliferating infantile haemangiomas: British Society for Paediatric Dermatology consensus guidelines. *Br J Dermatol*2018;179:582-9.

37. Chang L, Gu Y, Yu Z, et al. When to stop propranolol for infantile hemangioma. *Sci Rep* 2017;7:43292.

38. Fernandez Faith E, Shah S, Witman PM, et al. Clinical Features, Prognostic Factors, and Treatment Interventions for Ulceration in Patients With Infantile Hemangioma. *JAMA Dermatol*2021;157:566-72.

TABLE 1. Characteristics of respondents

Question	Responses	Results (N = 29 unless otherwise noted)
What is your medical degree?	MD/DO or equivalent Nurse Practitioner Physician Assistant	27 (93.1%) 2 (6.9%) 0
How long have you been practicing (years since training completed)?	< 10 years 10 – 20 years > 20 years	10 (34.5%) 7 (24.1%) 12 (41.4%)
Where do you live?	North America Asia	28 (96.6%) 1 (3.4%)
Which best describes your institutional size? (Descriptions are for pediatric hematology/oncology)	Small (fewer than 60 new oncology patients per year; 1-3 physicians) Medium (60 – 150 new oncology patients per year; 4-10 physicians) Large (More than 150 new oncology patients per year; more than 10 physicians)	N = 27 2 (7.4%) 16 (59.3%) 9 (33.3%)
What is your primary area of practice?	Pediatric Hematology/Oncology Dermatology Pediatric Cardiology Ophthalmology Other (Neonatology)	15 (51.7%) 2 (6.9%) 10 (34.5%) 1 (3.4%) 1 (3.4%)
At your institution, which discipline treats the majority of patients with infantile hemangiomas?	Pediatric hematology/oncology Dermatology Pediatric Cardiology Plastic surgery Otolaryngology General Pediatrics Combination	12 (41.4%) 11 (37.9%) 1 (3.4%) 0 0 1 (3.4%) 4 (13.8%)

TABLE 2. Summary of key responses

Scenario	**Results**
Most common scenarios receiving medical treatment	Infant with growing infantile hemangioma of the head/neck (74.1%)
Most common scenarios NOT receiving medical treatment	Older age (59.3%), though upper age limits variable from 6 months to 5 years Infant with multiple tiny lesions (84.6%) Older infant with non-growing lesion (84.6%) Small scalp lesion (53.8%)
Most common reasons for close monitoring and/or hospitalization	Infant < 5 weeks corrected gestational age (64.3%) PHACE syndrome (35.7%) high-risk social situation (39.3%)
Most common duration of outpatient observation	2 hours (39.3%), with monitoring of blood pressure (75%) and heart rate (67.9%)
Most common drug used	Generic propranolol (65.4%)
Most common dosing used	2 mg/kg/day (67.9%) divided in two doses (57.1%)

Scenario	Results
Typical frequency of follow-up evaluations	Every 4 weeks (56%)
Most common duration of therapy	Until 1 year of age (57.7%)
Most common method of discontinuation	Taper (53.8%) over 4 weeks (40%)

TABLE 3. Hypothetical cases and management scenarios

Hypothetical cases and scenarios	Responses	Results	Selected comments
For patients referred to you/your clinic with infantile hemangiomas, which treatment approach do you currently use most often?	Observation alone Propranolol (oral) Timolol (topical) Steroids (oral) Steroids (intralesional) Pulse dye laser therapy Referral to another practitioner Other	N = 29 2 (6.9%) 18 (62.1%) 5 (17.2%) 0 0 0 3 (10.3%) 1 (3.4%) (atenolol)	
An infant is less than 5 weeks gestationally-corrected age, has a sizeable, growing infantile hemangioma on the *trunk or extremity*, and is otherwise healthy. Would you recommend propranolol therapy for this patient?	Yes, usually Yes, but only if it was causing problems (such as ulceration, bleeding, etc.) No, I would wait until the patient is at least 5 weeks gestationally-corrected age (or older)	N = 27 12 (44.4%) 12 (44.4%) 3 (11.1%)	Truly depends on type of hemangioma; risk of ulceration not mentioned. We use atenolol, not propranolol, due to superior safety profile and equivalent efficacy.
An infant is less than 5 weeks gestationally-corrected age, has a sizeable, growing infantile hemangioma in the *head and neck region*, and is otherwise healthy. Would you recommend propranolol therapy for this patient?	Yes, usually Yes, but only if it was causing problems (such as ulceration, bleeding, etc.) No, I would wait until the patient is at least 5 weeks gestationally-corrected age (or older)	N = 27 20 (74.1%) 7 (25.9%) 0	Truly depends on type of hemangioma. We use atenolol, not propranolol, due to superior safety profile and equivalent efficacy.
If you treat (or recommend treatment for) an infant who is less than 5 weeks gestationally-corrected age, and that patient is already an outpatient, do you monitor the patient more closely than older infants?	Yes, in the hospital Yes, as an outpatient No, I usually monitor them the same as older infants Not applicable (I do not treat infants who are less than 5 weeks gestationally-corrected age.)	N = 29 17 (58.6%) 7 (24.1%) 4 (13.8%) 1 (3.4%)	

Hypothetical cases and scenarios	Responses	Results	Selected comments
For infants who are otherwise healthy and have a reassuring history and exam, how often do you administer the first dose of propranolol under medical supervision (e.g. in the clinic or hospital)?	Almost always Sometimes Rarely or never	N = 27 17 (63%) 1 (3.7%) 9 (33.3%)	I usually see medically complex hemangiomas. Dermatology sees term, uncomplicated patients with hemangiomas. All who are under 8 weeks corrected gestational age get admitted for initiation (24 hour observation) One in my 20 years. We don't admit to start propranolol any more - all started in clinic.
If you administer the first dose of propranolol under medical supervision (e.g. in the clinic or hospital), how long do you monitor patients?	One hour Two hours Overnight Other: Not applicable (I do not administer the first dose of propranolol under medical supervision.)	N = 28 2 (7.1%) 11 (39.3%) 3 (10.7%) 5 (17.9%) 7 (25%)	45 minutes About 2-3 hours 4 hours For under 3 months: slowly up titrate inpatient over 3 days. It depends on the age and/or gestational age. It depends on the reason for admission and other factors.
If you administer the first dose of propranolol under medical supervision (e.g. in the clinic or hospital), what do you typically monitor? (Select all that apply.)	Blood pressure Heart rate Glucose Other Not applicable (I do not administer the first dose of propranolol under medical supervision.)	N = 28 21 (75%) 19 (67.9%) 11 (39.3%) 1 (3.6%) 7 (25%)	Other = pulse ox
Approximately what percentage of your patients are admitted to the hospital to start propranolol?	< 10% 10 – 50% 50 – 90% > 90%	N= 27 23 (85.2%) 3 (11.1%) 1 (3.7%) 0	Need more information. Is it a high risk PHACE patient? Are there any other issues with the ulcerated hemangioma? Patients with other chronic medical conditions (congenital heart disease, chronic lung disease on oxygen, short gut syndrome)
A two-month-old full term infant has five small, scattered infantile hemangiomas on the trunk and extremities. Would you order a liver ultrasound for this patient?	Yes No Maybe	N = 27 20 (74.1%) 1 (3.7%) 6 (22.2%)	Only if signs/symptoms concerning for heart failure or hypothyroidism. If liver was large. Would have [primary care provider] or dermatology order.

Hypothetical cases and scenarios	Responses	Results	Selected comments
Which of the following situations would you be likely to recommend observation only? (Select all that apply.)	2 month old full term infant with an infantile hemangioma < 2 cm on the scalp 2 month old full term infant with an infantile hemangioma < 2 cm on the back, trunk, or extremity 2 month old full term infant with several small cutaneous hemangiomas, no liver involvement. 6 month old full term infant with an infantile hemangioma of the trunk or extremities with no significant growth in recent weeks.	N = 29 14 (53.8%) 19 (73.1%) 22 (84.6%) 22 (84.6%)	I use shared decision making with the parents/family. It really depends on location on the scalp and height and quality of lesion in all locations. Scalp one depends on appearance - more raised ones can cause permanent follicular damage. Very difficult to answer for the first two examples. Would depend on location, presence of ulceration or other complications.
Is there an approximate upper age limit at which you would *not* recommend treatment?	No (no upper age limit) Yes (please specify)	N = 27 11 (40.7%) 16 (59.3%)	6 – 9 months 8 months 9-12 months; hemangioma in plateau phase. 12 months 2 years Depends on lesion perhaps more than age; [rarely] after age 24 months. 4 years I would consider at almost all ages but less likely if older than 5. Would at least try if affecting child psychosocially.
For infants who are otherwise healthy and have a reassuring history and exam (you do not suspect liver involvement), before starting treatment, how often do you get lab work?	Most of the time Sometimes Rarely or never	N = 26 2 (7.7%) 4 (15.4%) 20 (76.9%)	
For infants who are otherwise healthy and have a reassuring history and exam (you do not suspect liver involvement), which labs do you typically get? (Select all that apply.)	Glucose Basic metabolic profile (BMP) Complete metabolic profile (CMP) Complete blood count (CBC) Thyroid function tests Other Not applicable (I do not get lab work pre-treatment.)	N = 26 5 (19.2%) 1 (3.8%) 1 (3.8%) 3 (11.5%) 1 (3.8%) 1 (3.8%) 20 (76.9%)	

Hypothetical cases and scenarios	Responses	Results	Selected comments
Before starting treatment, do you take baseline photographs (for the electronic medical records)?	Almost always Sometimes Rarely or never	N = 27 24 (88.9%) 2 (7.4%) 1 (3.7%)	
For infants who are otherwise healthy and have a reassuring history and exam, before starting treatment, how often do you get a pediatric cardiology consult?	Almost always Sometimes Rarely or never	N = 27 7 (25.9%) 3 (11.1%) 17 (63%)	
For infants who are otherwise healthy and have a reassuring history and exam (you do not suspect PHACE syndrome), before starting treatment, how often do you get an echocardiogram ("echo")?	Almost always Sometimes Rarely or never	N = 27 5 (19.2%) 4 (15.4%) 17 (63%)	
For infants who are otherwise healthy and have a reassuring history and exam (you do not suspect PHACE syndrome), before starting treatment, how often do you get an electrocardiogram (EKG)?	Almost always Sometimes Rarely or never	N = 27 9 (34.6%) 2 (7.7%) 15 (57.7%)	
If a patient is already an outpatient and has no vision or airway-threatening lesion, which patients would you currently admit to the hospital to start propranolol? (Select all that apply.)	None/almost none Patients with PHACE syndrome Infants less than 5 weeks gestationally corrected age Patients with ulcerated, painful, or mildly bleeding hemangiomas Patients with poor social situations I admit all patients to start propranolol Other	N = 28 7 (25%) 10 (35.7%) 18 (64.3%) 4 (14.3%) 11 (39.3%) 0 2 (7.1%)	

Hypothetical cases and scenarios	Responses	Results	Selected comments
In most cases, do you initially prescribe generic propranolol or trade name propranolol (Hemangeol®)?	generic propranolol Hemangeol® Neither/not applicable	N = 28 20 (71.4%) 7 (25%) 1 (3,6%)	Hemangeol® is convenient, but [very expensive], so I never prescribe it.
To the best of your knowledge, how easy is it for families to obtain propranolol?	Very easy Somewhat easy Not at all easy	N = 29 27 (93.1%) 2 (6.9%) 0	
To the best of your knowledge, how easy is it for families to get propranolol covered by their insurance?	Very easy Somewhat easy Not at all easy	N = 29 25 (86.2%) 4 (13.8%) 0	
To the best of your knowledge, which of these statements best fits your practice/experience?	Generic propranolol is easier to prescribe/obtain than Hemangeol®. Hemangeol® is easier to prescribe/obtain than generic propranolol. Generic propranolol and Hemangeol® are equivalent to prescribe/obtain.	N = 26 17 (65.4%) 1 (11.5%) 6 (23.1%)	
If you decide to admit a patient to the hospital to initiate therapy, how long do you typically keep the child in the hospital?	Overnight (24 hours or less) Two to three days Longer than three days Other Not applicable (I rarely or never admit patients to the hospital to initiate therapy.)	N = 28 10 (35.7%) 8 (28.6%) 0 1 (3.6%) 9 (32.1%)	It depends on the reason for admission and other factors.
If a patient is already an outpatient and has no vision or airway-threatening lesion, which patients would you currently admit to the hospital to start propranolol? (Select all that apply.)	None/almost none Patients with PHACE syndrome Infants less than 5 weeks gestationally corrected age Patients with ulcerated, painful, or mildly bleeding hemangiomas Patients with poor social situations I admit all patients to start propranolol. Other	N = 28 7 (25%) 10 (35.7%) 18 (64.3%) 4 (14.3%) 11 (39.3%) 0 2 (7.1%)	
For most patients, what is your usual *starting daily dose* of propranolol?	< 1 mg/kg/day 1 mg/kg/day 2 mg/kg/day 3 mg/kg/day Other	N = 28 3 (10.7%) 21 (75%) 4 (14.3%) 0	

Hypothetical cases and scenarios	Responses	Results	Selected comments
For most patients, what is your usual goal (full) dose of propranolol?	1 mg/kg/day 2 mg/kg/day 2.5 mg/kg/day 3 mg/kg/day Other	N = 28 0 19 (67.9%) 2 (7.1%) 7 (25%) 0	
Assuming no significant side effects, how quickly do you increase to the full dose (goal dose) of propranolol?	One week Two weeks Three weeks Four weeks Longer than four weeks I start with full dose on day one. Other	N = 26 6 (23.1%) 11 (42.3%) 3 (11.5%)) 2 (7.7%) 0 2 (7.7%) 2 (7.7%)	
How do you typically divide the total daily dose of propranolol?	Once a day (not divided) Two times a day Three times a day Other	N = 28 0 16 (57.1%) 10 (35.7%) 2 (7.1%)	2 times a day except for PHACE and those less than 5 weeks. Start TID until mom back to work then BID.
In your experience, approximately what percentage of the time do you or the families discontinue propranolol due to side effects?	Less than 5% 5 – 10% More than 10%	N = 25 19 (76%) 6 (24%) 0	We use atenolol almost exclusively and stop way less than 5% of the time. Often perceived side effect by parent has another cause.
In your experience, how often do you switch from one form of propranolol (generic or Hemangeol®), to the other form due to side effects or difficulty with administration?	Rarely Sometimes Frequently	N = 26 24 (92.3%) 2 (7.7%) 0	I have switched multiple patients from propranolol to atenolol because of reactive airway problems and it is much better tolerated.
What is the *typical* interval for the patient's next follow up visit (first outpatient visit after starting propranolol)?	One week Two weeks Four weeks/one month Two months Other	N = 26 6 (23.1%) 6 (23.1%) 13 (50%) 1 (3.8%) 0	
What is the *typical* interval for the patient's follow up visit starting with the third outpatient visit (second outpatient visit after starting propranolol)?	One week Two weeks Four weeks/one month Two months Other	N = 25 0 2 (8%) 14 (56%) 8 (32%) 1 (4%)	
Have you ever started propranolol using a telehealth encounter only?	Yes No	N = 26 7 (26.9%) 19 (73.1%)	During Covid lockdown, many patients were started via telehealth. Will do the consult by telehealth but always first dose in clinic.

Hypothetical cases and scenarios	Responses	Results	Selected comments
Are you currently using telehealth encounters for routine follow up visits?	Yes No	N = 25 16 (64%) 9 (36%)	[For] patients with difficulty coming to clinic visits, [we] use telehealth and frequent nursing telephone calls. Yes and no; sometimes depending on patient preference. Only if I can get good photos and an accurate weight, but often I can.
How often do you provide oral syringes to the parents?	Always Sometimes Rarely or never	N = 27 17 (63%) 3 (11.1%) 7 (25.9%)	They are part of the Hemangeol® box. Absolutely. And make certain parents are knowledgeable regarding proper dosing. Pharmacy does this.
How often do you teach or instruct a parent how to use an oral syringe and how to draw up the prescribed dose?	Always Sometimes Rarely or never	N = 27 17 (63%) 4 (14.8%) 6 (22.2%)	Always
When starting propranolol, how do you educate parents?	Verbally only Verbally, plus a printed handout (information sheet, brochure or pamphlet) Verbally, a printed handout, and a web site recommendation Other	N = 28 11 (39.3%) 0 13 (46.4%) 2 (7.1%) 2 (7.1%)	Verbally and individual treatment plan for each patient. Verbally and via electronic messaging.

Hypothetical cases and scenarios	Responses	Results	Selected comments
If you provide a printed handout for the parents, which one do you provide?	From the pedsderm.net web site From the publication in *Pediatric Dermatol*ogy (Martin K et al. Propranolol treatment of infantile hemangiomas: anticipatory guidance for parents and caretakers *Pediatr Dermatol.* 2013 Jan-Feb;30(1):155-9. Doi: 10.1111/pde.12022) Pierre Fabre pamphlet "Facts you should know about infantile hemangioma: Guidance for Parents" I provide an institution-specific and/or custom-made handout Not applicable (I do not provide an information handout for the parents.)	N = 24 1 (4.2%) 1 (4.2%) 2 (8.3%)) 12 (50%) 8 (33.3%)	
Do you recommend any specific web site(s) for parents about infantile hemangioma and/or propranolol?	Yes (please specify) No	N = 28 3 (10.7%) 25 (89.3%)	Hemangioma Investigator Group, Pediatric Dermatology website, few others Ours and Hemangioma Investigator Group National Organization of Vascular Anomalies.
For most patients, what is the *typical* time at which you discontinue propranolol?	After six months of therapy, regardless of patient's age Approximately one year of age Approximately 15 months of age Other	N = 26 2 (7.7%) 15 (57.7%) 7 (26.9%) 2 (7.7%)	Wean at 12 months Totally dependent on type of hemangioma - often add topical and/or drop second dose and add topical.
When discontinuing propranolol, do you...	Discontinue it abruptly Taper it Let the patient outgrow the dose and then stop it at some point in the future Let the parent(s) decide when to stop Other	N = 26 4 (15.4%) 14 (53.8%) 7 (26.9%) 0 1 (3.8%)	Outgrow then taper
If you taper the dose off, what is the typical length of the taper?	One week Two weeks Four weeks/one month Not applicable (I do not taper) Other	N = 25 2 (8%) 6 (24%) 10 (40%) 6 (24%) 1 (4%)	Other = 3 weeks

Hypothetical cases and scenarios	Responses	Results	Selected comments
After discontinuing propranolol, what is your typical follow up strategy?	Reassess the patient in clinic at least one more time, off therapy Discharge from your practice and have the patient follow up with his/her primary care provider Other	N = 26 17 (65.4%) 7 (26.9%) 2 (7.7%)	Reassess one time physically and then calls over a year (non billed). Have the family call us if they see the hemangioma start to regrow or get redder after propranolol stopped.
Other comments			Each patient and each hemangioma is a bit different - treatment is very specific to type of hemangioma and/or if there is ulceration, risk of ulceration, visual issues, etc. Important to recognize which patients warrant further evaluation.